having a particularly high level of homology with respect to the probe sequences. High stringency conditions comprise a temperature of about 42°C or less, a form amide concentration of less than about 20%, and a low salt (SSC) concentration. Alternatively they may comprise a temperature of about 65°C or less, and a low salt (SSPE) concentration. Preferred conditions for such screening comprise a temperature of about 42°C, a formamide concentration of about 20%, and a salt concentration of about 2 X SSC, or a temperature of about 65°C, and a salt concentration of about 0.2 SSPE.

Copies of the marked-up versions of the present specification amendments are attached.

REMARKS

The Official Communication dated November 27, 2002 indicates that the Amendment and Request for Consideration Under 37 C.F.R. §1.111, filed by applicants on September 12, 2002, is not fully responsive in that a protein sequence appears in Figure 4 which is not identified by an appropriate sequence identifier in the Brief Description of the Figures appearing at page 22 of the specification, and that new drawings were not submitted as required in the March 12, 2002 Official Action.

In accordance with the present amendment, the brief description of Figure 4 has been amended to make reference to a sequence identifier for the protein sequence appearing in Figure

4, which is identified as Figures 4A-4L. A consequential amendment has been made at page 29 of the specification.

As for the new drawing requirement, applicants respectfully direct the Examiner's attention to §1893.03(f) of the Manual of Patent Examining Procedure ("Drawings and PCT Rule 11"), which provides in pertinent part:

> The drawings for the national stage application must comply with PCT Rule 11. The copy of the drawings provided by the International Bureau has already been checked and should be in compliance with PCT Rule 11. Accordingly, the drawings provided by the International Bureau should be acceptable....The Official Draftsman may not impose requirements beyond those imposed by the Patent Cooperation Treaty (e.g. PCT Rule 11). The examiner does indeed have the authority to require new or more acceptable drawings if the drawings were published without meeting all requirements under the PCT for drawings...(emphasis added).

In the present case, neither the Official Draftsperson nor the Examiner has indicated that the drawings provided by the International Bureau fail to meet any specific drawing requirement under the Patent Cooperation Treaty. The objections indicated in the Notice of Draftperson's Patent Drawing Review are made with reference to 37 C.F.R. and not Rule 11 of the Patent Cooperation Treaty. Nevertheless, in the interest of advancing the prosecution of this application, applicants are submitting herewith new Figures 1-8 on seventeen (17) sheets (rather than sixteen (16)) showing proposed changes in red for approval by the Examiner in accordance with 37 C.F.R. §1.121(d). Upon approval of the proposed changes by the Examiner, new drawings including these changes will be submitted.

Applicants once again request favorable reconsideration of the present application.

Respectfully submitted,

DANN DORFMAN HERRELL and
SKILLMAN, P.C.
Attorneys for Applicant

By Patrick J. Hagan
Patrick J. Hagan
Registration No. 27,643

PJH:ksk

Marked-Up Version of Replacement Paragraphs

Figures 4A-4L - show[s] the complete listing of the R. corallina ohp operon as described in Example 7 (SEQ ID No. 1 - top strand; SEQ ID No. 2 - bottom strand). It includes a portion of a putative nitropropane promoter ([51] 5' of the regulator; amino acid sequence shown in SEQ ID No. 3).

Example 6: Hybridisation screening for novel promoters and/or operon proteins

The test sample (host cells) are contacted with a nucleic acid molecule probe (preferably around 100 nucleotides or more) based on Figures 4A-4L under suitable hybridisation conditions, and any test DNA which hybridises thereto is identified. Such screening is initially carried out under low-stringency conditions, which comprise a temperature of about 37°C or less, a formamide concentration of less than about 50%, and a moderate to low salt (e.g. Standard Saline Citrate ('SSC') = 0.15 M sodium chloride; 0.15 M sodium citrate; pH 7) concentration. Alternatively, a temperature of about 50°C or less and a high salt (e.g. 'SSPE' = 0.180 mM sodium chloride; 9 mM disodium hydrogen phosphate; 9 mM sodium dihydrogen phosphate; 1 mM sodium EDTA; pH 7.4). Preferably the screening is carried out at about 37°C, a formamide concentration of about 20%, and a salt concentration of about 5 X SSC, or a temperature of about 50°C and a salt concentration of about 2 X SSPE. These

conditions will allow the identification of sequences which have a substantial degree of similarity with the probe sequence, without requiring the perfect homology for the identification of a stable hybrid. The phrase 'substantial similarity' refers to sequences which share at least 50% overall sequence identity. Preferably, hybridisation conditions will be selected which allow the identification of sequences having at least 70% sequence identity with the probe, while discriminating against sequences which have a lower level of sequence identity with respect to the probe. After low stringency hybridisation has been used to identify several clones having a substantial degree of similarity with the probe sequence, this subset of clones is then subjected to high stringency hybridisation, so as to identify those clones having a particularly high level of homology with respect to the probe sequences. High stringency conditions comprise a temperature of about 42°C or less, a form amide concentration of less than about 20%, and a low salt (SSC) concentration. Alternatively they may comprise a temperature of about 65°C or less, and a low salt (SSPE) concentration. Preferred conditions for such screening comprise a temperature of about 42°C, a formamide concentration of about 20%, and a salt concentration of about 2 X SSC, or a temperature of about 65°C, and a salt concentration of about 0.2 SSPE.